REMARKS

A. Claim Amendments.

Claim 1 has been amended to recite that the nucleic acid claimed is "isolated." No new matter is added by this amendment, entry of which is therefore requested.

B. Response to Rejection of Claims under 35 USC §101.

Claims 1 and 10-12 have been rejected as being drawn to non-statutory subject matter, in that Claim 1 is contended to encompass naturally occurring nucleic acids. The claim has now been amended to recite that the nucleic acids are isolated. Applicants appreciate the Examiner's suggestion in this regard, and respectfully submit that the non-statutory subject matter rejection should now be withdrawn.

C. Response to Rejection under 35 USC §102(a).

Claims 1 and 10-12 have been rejected as being anticipated by a paper co-authored by the inventors having a publication date less than one year before the filing date of this application (Wang, *et al.*). A declaration under 37 CFR § 1.131 with respect to the publication is submitted herewith, and establishes that the Wang, *et al.* paper does not represent knowledge or use of the invention "by others" (35 USC §102(a)). As such, Applicants respectfully submit that the Wang, *et al.* paper is not prior art to the present claims (*In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982)), and request that the rejection under §102(a) be withdrawn.

D. Response to Rejections under 35 USC §112, First Paragraph.

Claims 11 and 12 have been rejected for lack of enablement. Applicants respectfully disagree.

In particular, Claim 11 is rejected on the basis that "Claim 11 is so broad as to encompass host cells transformed with specific nucleic acids, including cell in *in vitro* culture as well as cells within any multicellular organism." (Office Action, at page 3, paragraph 5). It is said that "expression of genes in a particular host cell...having the desired biological characteristics is unpredictable [sic and] the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue." (Office Action at page 4). The Office Action only notes that only *in vitro* use of the nucleic acids is exemplified in the application (*ibid*).

Applicants note that no evidence, reference or other knowledge in the art is cited in the Office Action for any contrary conclusion. Therefore, Applicants submit that no *prima facie* case for non-enablement has been made (MPEP 2164.09; *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ2d 367,370, 1971). In particular, the record lacks explanation of what information considered necessary to enablement is missing and why one of ordinary skill in the art would need to engage in undue experimentation to supply it (MPEP 2164.06(a)). Nonetheless, for purposes of compact prosecution, Applicants will address the substance of the rejection as stated.

Applicants submit that no reason has been established to believe that one of ordinary skill in the art could not produce host cells comprising the claimed nucleic acids *in vitro* and *in vivo*. Firstly, it is not accurate to state that the application does not contemplate *in vivo* use of the nucleic acids; e.g., to transduce host cells *in situ*. To the contrary, one of the stated aims of the invention is to provide means for "gene augmentation therapy" using the nucleic acids of the invention, a goal those of ordinary skill in the art would immediately appreciate as being

achievable *in vivo* (e.g., by direct introduction of an expression vector containing the nucleic acid into host cells) or *ex vivo* (e.g., by implantation or grafting of host cells into a tissue).

Moreover, Applicants note that the claimed nucleic acids are isolated forms of a nucleic acid that occurs in, and is expressed by, cells in a wide range of tissues, including the heart, brain, placenta, lung, liver, skeletal muscle, kidney and pancreas (see, e.g., Figure 6A). There is no reason to believe that such cells could not be successfully transfected with the nucleic acids claimed using conventional techniques. Further, although expression is not a requisite limitation of Claim 11 (which is directed only to cells comprising the nucleic acid, not expressing a protein), there is no reason to believe that the expression vectors of enabled Claim 10 could not be utilized to that end.

In this respect, to be enabling, the application must teach those skilled in the art how to make and use the full scope of the claimed invention without *undue* experimentation, not *no* experimentation. *Genentech, Inc. v. Novo Nodisk A/S*, 108 F.3d 1361, 1365, 42 U.S.P.Q.2d 1001, 1004 (Fed. Cir. 1997), *see also* MPEP §2164.01(c), fourth paragraph. Routine experimentation does <u>not</u> constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention as claimed.

(*Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360 (Fed. Cir. 1998), *citing PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996); *see also In re Wands*, 858 F.2d 731, 736-40 (Fed. Cir. 1988)).

Applicants submit that, in view of the foregoing, the effort to successfully transfect cells within and outside of a host would require only routine experimentation, using conventional techniques. For example, those of ordinary skill in the art would immediately comprehend that, using an expression vector of Claim 10, one could inject the vector into host cells by a technique such as those described in the art; e.g., non-vector based methods include nonviral physical transfection of DNA into cells; for example, microinjection (DePamphilis et al., *BioTechnique* 6:662-680 (1988)); electroporation (Tonequzzo et al., *Molec. Cell. Biol.* 6:703-706 (1986), Potter, *Anal. Biochem.* 174:: 361-33 (1988)); chemically mediated transfection such as calcium phosphate transfection (Chen and Okayama, *Mol. Cell. Biol.* 7:2745-2752 (1987), Chen and Okayama, *BioTechnique*, 6:632-638 (1988)) and DEAE-dextran mediated transfer (McCutchan and Pagano, J *Natl. Cancer Inst.* 41:351-357 (1968)); cationic liposomal mediated transfection (Felgner et al., *Proc. Natl. Acad. Sci. USA*, 84:7413-7417 (1987), Felgner and Holm, *Focus* 11:21-25 (1989) and Felgner et al., *Proc. West. Pharmacol.* Soc. 32:115-121 (1989)) and other methods known in the art.

For *in vivo* use, construction of vectors for recombinant expression of nerve growth factors for use in the invention may be accomplished using conventional techniques which do not require detailed explanation to one of ordinary skill in the art as described in, for example, Maniatis et al., in Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York (1982). Adenovirus, adeno-associated virus and lentivirus are all viral vectors that are known to be useful for achieving stable transfection of a variety of cells, including non-dividing cells, and can be readily employed to produce vector compositions useful in the claimed invention (for reference, see, e.g., Straus, The Adenovirus, Plenum Press (NY 1984), pp. 451-496; Rosenfeld, et al., *Science,* 252:431-434 (1991); U.S. Pat. No. 5,707,618 [adenovirus vectors for use in gene therapy]; and U.S. Pat. No. 5,637,456 [method for determining the amount of functionally active adenovirus in a vector stock], the contents of each of which is incorporated herein to illustrate

the level of skill in the art). Such compositions can also be readily delivered by means including microinjection through a surgical incision (see, e.g., Capecchi, *Cell,* 22:479-488 (1980)); electropotation (see, e.g., Andreason and Evans, *Biotechniques*, 6:650-660 (1988)); infusion, chemical complexation with a targeting molecule or co-precipitant (e.g., liposome, calcium), and microparticle bombardment of the target tissue (Tang, et al., *Nature,* 356:152-154 (1992)).

Applicants respectfully submit that no reason has been established to believe that methods such as those described above could not be utilized with the nucleic acids of the invention. Moreover, as already stated, such methods are not express limitations on the invention as claimed, which can be practiced simply by introducing a nucleic acid of Claim 1 into a host cell.

For all of these reasons, reconsideration and withdrawal of the rejection of Claim 11 under §112, first paragraph is therefore requested.

As to Claim 12, the rejection made contends that "[t]here is no evidence presented that [a nucleice acid of the invention] is associated with any of the known diseases or disorders or can be treated by administering the nucleic acid." It is noted that no evidence or reference is cited in the Office Action for any contrary conclusion. Therefore, Applicants submit that no *prima facie* case for non-enablement has been made (MPEP 2164.09; *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ2d 367, 370, 1971). In particular, the record lacks explanation of what information considered necessary to enablement is missing and why one of ordinary skill in the art would need to engage in undue experimentation to supply it (MPEP 2164.06(a)). Nonetheless, for purposes of compact prosecution, Applicants will address the substance of the rejection as stated.

Applicants respectfully submit that the rejection turns on limitations that are not present in the claim; i.e., method of use limitations drawn to treating a disease or disorder. Just as a claimed structure cannot be defined by its function, a claimed structure cannot be rejected on the basis of functional limitations not present in the claim (see, e.g., MPEP 2111.01(II) [limitations present only in the Specification cannot be read into the claims]; MPEP 2114 [article claims are judged on their structural characteristics, not functional ones]). Further, as a practical matter, even if functional limitations not present could properly be read into a claim for purposes of an enablement inquiry, there is no logical reason why the limitations would have to require treatment of a "disease or disorder." To the contrary, pharmaceutical preparations may be utilized to prevent occurrence of a disease or disorder, to maintain a state or condition in a patient, or in research. Whatever *use* is eventually made of a pharmaceutical composition, whether or not its preparation is enabled under §112, first paragraph depends only on whether the application provides sufficient structural information to allow one of ordinary skill in the art to produce the formulation without undue experimentation.

Here, the structural characteristics of the invention of Claim 12 are clear. The compositions claimed consist of a pharmaceutically acceptable carrier and a nucleic acid of Claim 1. Claim 1 being enabled for the nucleic acid, one of ordinary skill in the art can be expected to have no difficulty whatsoever identifying a pharmaceutically acceptable carrier and placing the nucleic acid into it. As such, the claim *as it is written* is enabled, irrespective of the nature of any subsequent use that might or might not be made of the claimed composition. Reconsideration and withdrawal of the rejection of Claim 12 under §112, first paragraph is therefore requested.

CONCLUSION

Applicants respectfully submit that that the claims are now in condition for allowance. Favorable consideration of Claims 1 and 10-12 is hereby requested. If the Examiner believes that prosecution can be advanced further by discussion of the issues addressed herein, the undersigned may be contacted by phone at 858 677-1423.

Check No. 585983 in the amount of $510.00 is enclosed for the Petition for a Three-Month Extension of Time Fee. No other fee is believed to be due in connection with filing this paper. However, the Commissioner is hereby authorized to charge any other fees that may be required by this paper or credit any overpayment to Deposit Account 07-1896 referencing the above-identified attorney docket number. A duplicate copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

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